PATENT

Attorney Docket No.: A-67616-1/RMS/DCF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

STUELPNAGEL et al.

Serial No. 09/500,555

Filed: February 9, 2000

For: AUTOMATED INFORMATION PROCESSING IN RANDOMLY ORDERED ARRAYS

Examiner: B.J. Forman

Group Art Unit: 1655

COPY

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Signed: _____

Fern S. Marder

AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Dear Sir:

This amendment is in response to the Office Action dated April 20, 2001. The amendment is accompanied by a petition for a three month extension of time and the required fee, making this a timely response.

Please amend the above-identified application as follows:

In the Claims:

Please delete claims 13-17 and 28-43 without prejudice or disclaimer as being drawn to a non-elected invention. Please amend the claims as follows:

1. (Amended) An array composition comprising:

a) a substrate with a surface comprising discrete sites; and

b) a population of microspheres comprising at least a first and a second subpopulation, wherein each subpopulation comprises a bioactive agent; and

c) at least one fiducial;

wherein said microspheres are distributed on said surface.

3. (amended) An array composition according to claim 1 wherein each subpopulation comprises an identifier binding ligand that will bind a decoder binding ligand for identification and elucidation of the bioactive agent.

19. (amended) A method according to claim 18 wherein said subpopulations further comprise an identifier binding ligand that will bind a decoder binding ligand for identification and elucidation of the bioactive agent.

20. (amended) A method according to claim 18 wherein said subpopulations further comprise an optical signature for identification and elucidation of the bioactive agent.

28. (new) A composition according to claim 1, wherein said discrete sites are wells.

29. (new) A composition according to claim 1, wherein said microspheres are randomly distributed on said substrate.

30. (new) A method according to claim 18, wherein said discrete sites are wells.

31. (new) A method according to claim 18, wherein said microspheres are randomly distributed on said substrate.

REMARKS

Claims 1-12, 18-31 are now pending in the application.

Claim 1 was amended to correct the informality of the claim. Claims 3, 19 and 20 are amended according to the Examiner's suggestions to recite with more particularity that which Applicants regard as their invention. Claims 28-31 are new claims. Support for claim 28 and 30 is found throughout the specification, for instance on page 6, lines 17-18; page 7, lines 14-24. Support for claims 29 and 31 are found throughout the specification, for instance, on page 9, lines 27-31.

Changes in the amendment are shown in the Versions Showing Changes in the Amendment appended to this response. For the Examiner's convenience, a copy of the currently pending claims is also appended as "Pending Claims".

Election/Restrictions

Applicants confirm that Group I of the claims, i.e., claims 1-12, 18-27 are elected for further prosecution. Claims 13-17, 28-43 are cancelled with prejudice or disclaimer.

Claim objections on informality

Claim 1 is rejected because of informality. Applicant has correspondingly made the required corrections, and respectfully request that the rejection be withdrawn.

Claim rejections - 35 U.S.C. §112

Claims 3, 19 and 20 are rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant has correspondingly amended the claims according to the Examiner's suggestion. The claims should now be in a condition for allowance. Therefore, Applicant respectfully request that the rejection be withdrawn.

Claim rejection - 35 U.S.C. §103

Claims 1-10 & 18-27 are rejected under 35 U.S.C. §103(a) as being unpatentable over Walt et al.(U.S. Patent No. 6,023,540, "Walt") in view of Augenlicht, L. (U.S. Patent no. 4,981,783, "Augenlicht").

Walt teaches a microsphere-based analytic chemistry system comprising a substrate with a surface comprising discrete sites and a population of microspheres with chemical functionalities wherein said microspheres are distributed on the surface of the substrate. Regarding claims 1 and 18, Walt is silent with respect to teaching an array composition comprising at least one fiducial.

Augenlicht teaches a method of determining the expression of individual cloned genes that are stored in a defined pattern on substrates such as nitrocellulose filters and teaches the uses of fiducial markings to identify the position of individual clones on the filter relative to the fiducial. Part of the reason Augenlicht uses the fiducial markings is because the growth of the clones is variable; see column 8, line 31. Augenlicht does not teach or suggest the use of fiducial in an array comprising microspheres, which can be randomly arranged on a substrate.

The present invention discloses an array composition and a method of making an array composition that comprises a substrate with a surface comprising discrete sites; a population of microspheres comprising bioactive agents wherein said microspheres are distributed on the surface of the substrate; and at least one fiducial. The fiducial are used to generate registered data images, and the comparison among the images can then lead to the identification and elucidation of the bioactive agent.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestions or motivation, whether in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or reference when combined) must teach or suggest all the claim limitations. (see M.P.E.P. §2143).

The Examiner states that the motivation to combine the references is for "the expected benefit of facilitating analysis and identification of the bioagents by identifying their position

on the substrate relative to the fiducial as taught by Augenlicht." However, the Applicants respectfully point out that this is not sufficient motivation under 35 U.S.C. §103, as the Examiner has failed to point to specific teachings in the references that would motivate the skilled artisan to add fiducials to the arrays of Walt.

As the Examiner is aware, a statement that "modifications of the prior art to meet the claimed invention would have been obvious to one of ordinary skill in the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). Therefore, Applicants respectfully submit that a *prima facie* case of obviousness has not been established in this case.

Similarly, with regard to claim 2 and 20, a *prima facie* case of obviousness has not been established because the Examiner failed to point to the teachings in either of the references that would have motivated the skilled artisan to combine the teachings of Walt and Augenlicht.

Regarding claims 3 and 19, Applicants respectfully submit that Walt is silent on teaching an identifier binding ligand and a decoder binding ligand. Thus, not every element of the claim have been disclosed. Furthermore, as discussed above, neither of the references has taught or suggested a motivation to combine the two references. Thus, a *prima facie* case of obviousness has not been established.

Regarding claims 4, 5, 6, 21, 22 and 23, as the examiner has stated, Walt does not teach or suggest a fiducial fiber. While Augenlicht has taught the use of a fiducial marker on a nitrocellulose filter, he did not teach suggest the use of a fiducial fiber. Thus, not every element of the claim have been disclosed by the two references. Furthermore, as discussed above, neither of the references has taught or suggested a motivation to combine the two references. Thus, a *prima facie* case of obviousness has not been established.

Regarding claims 7 and 24, as discussed above, because neither of the references have taught or suggested the motivation to use the fiducial taught in Augenicht in the microsphere-based system taught in Walt, a *prima facie* case of obviousness has not been established.

Regarding claims 8 and 25, as the examiner has stated, Walt does not teach or suggest a fiducial bead. While Augenlicht has taught the use of a fiducial marker on a nitrocellulose filter, it has not taught or suggested the use of a fiducial bead. Thus, not every element of the claim have been disclosed by the two references. Furthermore, as discussed above, neither of the references has taught or suggested a motivation to combine the two references. Thus, a *prima facie* case of obviousness has not been established.

Regarding claims 9, 10, 26 and 27, as discussed above, because neither of the references has taught or suggested the motivation to use the fiducial taught by Augenlicht in the microsphere-based system taught in Walt, a *prima facie* case of obviousness has not been established.

Regarding the new claims 28 and 30, as discussed above, because neither of the references has taught or suggested the motivation to use the fiducial taught by Augenlicht in the microsphere-based system taught in Walt, a *prima facie* case of obviousness has not been established.

Regarding the new claims 29 and 30, neither of the references has taught or suggested the motivation to use the fiducial taught by Augenlicht in the microsphere-based system taught in Walt. Furthermore, as mentioned above, Augenlicht teaches the use of fiducial to locate the position of a desired gene clone in an *ordered* filter set, while the present invention is directed to an array composition in which microspheres are *randomly distributed* on a substrate. Without specific teaching, one would not be motivated to use the fiducial taught in Augenlicht in a random array.

Claims 11-12 are rejected under 35 U.S.C. §103(a) as being unpatentable over Walt in view of Augenlicht and Chee et al. (U.S. Patent No. 5,795,716, "Chee").

Walt and Augenlicht are discussed above. Chee teaches the use of computer systems for visualizing biological sequences, as well as for evaluating and comparing biological sequences from a biological array.

Like Augenlicht and Walt, Chee does not teach or suggest the use of fiducial in an array comprising microspheres. Neither does Chee teach or suggest any motivation to combine the fiducial taught by Augenlicht with the array composition taught by Walt. Therefore, as discussed above, a *prima facie* case of obviousness has not been established.

Based on the above arguments, Applicants respectfully submit that a prima facie case of obviousness has not been established for any of the claims, and the rejections should be withdrawn. Furthermore, applicant submits that the claims are now in condition for allowance and an early notification of such is solicited.

Respectfully submitted,

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ALBRITTON & HERBERT LLP

Date: October 22, 2001

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